SQUAMOUS-CELL CARCINOMA OF THE RENAL PELVIS WITH SPECIAL REFERENCE TO ETIOLOGY

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FROM THE SURGICAL SERVICE OF THE ELLIS HOSPITAL

The rare incidence of primary renal pelvic tumors in general and the recent observation of two squamous-cell tumors prompts the following case reports and review of the literature.

Case I.—(No. 10338). Mrs. A. Y., white, married, aged fifty-six, was admitted to the Ellis Hospital March 13, 1933, with a chief complaint of pain in the right side of the abdomen and right back, of a year's duration. Recently the pain had been accompanied by nausea, vomiting and profuse sweating. Eleven weeks previous to admission the gall-bladder was drained in another hospital but without relief of symptoms. The patient continued to have dull, aching pain which extended from the right flank and anteriorly into the right lower quadrant. There was no frequency of urination, dysuria or hematuria. There was a gradual loss of twenty pounds in weight.

Physical examination disclosed an acutely ill, middle-aged woman. The examination was negative except for marked tenderness over the entire right lower abdomen and posteriorly to the right costovertebral angle as well as in the inner surface of the upper right thigh. A large mass was palpable, filling the right upper quadrant and extending posteriorly, which was firm, rounded, fixed and tender, and measured about fifteen by twenty centimetres.

Four days after admission to the hospital, the patient had an irregular septic temperature, at times as high as 103°, with a pulse of 135. Urinalysis was negative except for a faint trace of albumin and a moderate number of leucocytes. Blood count was red blood-cells, 3,200,000; white blood-cells, 14,000; 62 per cent. hæmoglobin (Newcomer); 82 per cent. polymorphonuclear leucocytes, 13 per cent. lymphocytes, 1 per cent. endothelial leucocytes, and 4 per cent. myelocytes. Blood Wassermann and Kahn tests negative. Blood sugar, 120 milligrams per 100 cubic centimetres, urea nitrogen, 16.5 milligrams per 100 cubic centimetres.

On the day of admission she was given a transfusion of 500 cubic centimetres of citrated blood. A flat X-ray plate was negative except for a small irregular shadow thought to be a calculus in the right kidney region. Cystoscopy disclosed a normal bladder. No urine was excreted from the right ureteral orifice. Clear urine was noted coming from the left ureter. A No. 6 ureteral catheter was easily passed to the right kidney pelvis and a pyelogram was made. The right pyelogram disclosed a large irregular mottled shadow without definite outlines and the smaller shadow previously noted, was seen in close relation to the catheter. A diagnosis was made of right perinephritic abscess with kidney calculus. Operation, March 17, 1933. A right Mayo incision immediately opened into a large perinephritic abscess filled with foul pus. The right kidney was found enlarged and almost entirely replaced by a pyonephrotic abscess cavity. The kidney substance was very adherent at the hilus and in an attempt to remove the organ, the peritoneal cavity was accidentally opened. Gauze was packed down to the opening, cigarette drains placed and the wound was closed. A right rectus incision was made and the peritoneal opening was identified just lateral to the ascending colon and closed. The peritoneum was drained and the wound closed in layers. A culture showed organisms of the gram-negative colon group.

The patient reacted poorly and died of sepsis and cardiac failure five days postoperative. An autopsy the same day disclosed a localized abscess cavity in the right colic gutter which communicated with the abscess cavity surrounding the right kidney. There were two other secondary collections of pus present which communicated with the primary abscess cavity. One cavity was subdiaphragmatic, ten centimetres in diameter, over the right lobe of the liver, and the other retroperitoneal sixteen centimetres in diameter extending beneath the ascending colon over to the mid-line. Cultures from the subdiaphragmatic abscess yielded hemolytic Staphylococcus aureus and B. coli communis. The right kidney, fifteen by ten by nine centimetres, was found in the medial portion of the perinephritic abscess, and consisted of a collapsed sac. Around the hilus and pelvis there was marked inflammatory thickening which resembled indurated fat or tumor tissue. In the lower portion of the pelvis there was an irregular blood-stained calculus of staghorn type, about one by three centimetres in diameter. The upper ureter was almost completely obliterated by dense, fibrous tissue. The middle and lower ureter was about twice normal in diameter and showed numerous rounded, raised areas in the mucosa which resembled atheromatous plaques. There was no evidence of distant metastases.

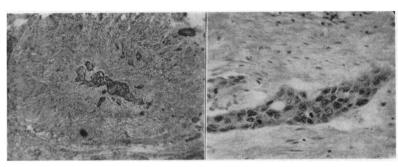


Fig. 1.—(Case I.) Low power, showing tumor embolus in small artery.

Fig. 2.—(Case I.) High power, tumor showing squamous-cell characteristics.

Microscopical examination of various portions of the kidney shows the remains of a few tubules and dense, fibrous tissue in which are many groups of tumor-cells, some arranged in the form of acini, others without differentiation. Mitoses are infrequent. An occasional area shows clusters of squamous epithelium. The blood-vessels show marked degenerative changes in which there are hyaline areas, intimal thickening and organized thrombi. The right ureteral wall is thickened and diffusely infiltrated with numerous clusters of tumor-cells having squamous epithelial characteristics, and marked lymphocytic infiltration.

Summary of Anatomical Diagnosis.—Chronic interstitial nephritis and squamous-cell carcinoma of right kidney and ureter, grade III. Infarct (fifteen centimetres) upper pole of the left kidney. Chronic pleuritis. Chronic myocarditis.

CASE II.—(No. 10244). Mr. A. P., married, white, farmer, aged fifty-four, entered the Ellis Hospital March 7, 1933, with a chief complaint of pain in the left kidney region.

For the past four months he had irregular attacks of sharp pain posteriorly in the left kidney region. Abdominal pain had also been present since the previous summer when it was aggravated by heavy farm work. He complained of no urological symptoms.

In his past history he had an attack of rheumatic fever at the age of twenty-two years, lasting six weeks, and an attack of influenza in 1918. In December, 1932, he complained of abdominal pains, constipation, and the passage of bloody stools, and a sensation of numbness extended down the left leg to the toes. A gastro-intestinal radiographical series at that time was negative. A few red blood-cells were found in urinalysis and cystoscopy

was recommended but not carried out. On admission, the physical examination was negative except for a firm, fixed, non-tender mass palpable in the left kidney region, extending well up under the costal margin.

Urinalysis on two examinations was negative except for a slight trace of albumin and occasional blood- and pus-cells. Phenolsulphonephthalein test showed 17 per cent. excretion in the first hour, 17 per cent. in the second hour; a total of 34 per cent. in two hours.

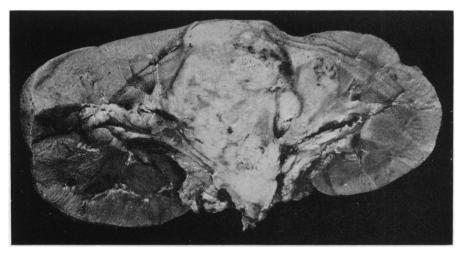


Fig. 3.—(Case II.) Bisected kidney showing pelvic origin of tumor.

The blood Wassermann and Kahn tests were negative. Blood sugar, 107 milligrams per 100 cubic centimetres, urea nitrogen, 13 milligrams per 100 cubic centimetres.

Cystoscopy disclosed a normal bladder. Ureteral catheters were passed easily and bilateral pyelograms were made. The right pyelogram was normal except for slight kinking of the right ureter at the level of the upper border of the fourth lumbar vertebra. The left kidney disclosed no iodide in the pelvis, although some was present in the upper and lower calyces. The ureter appeared somewhat dilated at the ureteropelvic junction.

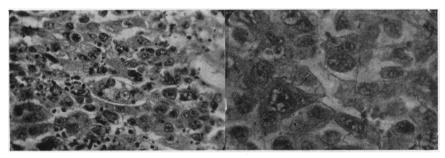


Fig. 4.—(Case II.) Low power, showing highly Fig. 5.—(Case II.) (Oil immersion.) Showing malignant anaplastic carcinoma of renal pelvis.

Clinical Diagnosis.—Primary tumor of the left kidney pelvis. Operation, March 13, 1933. Through the usual loin incision the left kidney was found enlarged and adherent. A hard mass replaced the middle third of the kidney and extended medially along the hilus, making mobilization difficult. Nephrectomy was carried out, but tumor tissue about the pedicle could not be completely removed.

The specimen consists of a bisected kidney, fourteen by seven by five centimetres. On section, a somewhat globular tumor mass is found in the middle third of the kidney. It

measures four centimetres in diameter and occupies the pelvic region extending from the pelvis through the kidney substance to the capsule on the outer border. Although the tumor is fairly sharply defined, there is no distinct capsule about the growth. The pelvic portion of the tumor infiltrates the peripelvic fat and surrounds the calyces, which are only moderately distorted. The cut surface is mottled, gray, white and red and interspersed with numerous minute yellowish puncta. The pelvic mucosa is cedematous, granular, and deeply injected.

Microscopical examination of sections of the tumor show a cellular actively infiltrating growth, composed of large cells having an epithelial character, and suggesting epidermoid cells. Differentiation is very poor and mitotic figures are abundant. The nuclei vary greatly

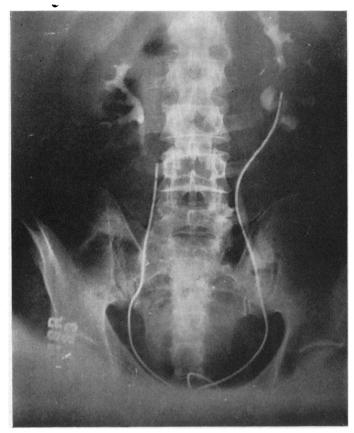


Fig. 6.—Pyelogram of second case showing deformity of kidney pelvis.

Diagnosis: primary pelvic tumor.

in size but tend toward large size; many macronuclei are observed and not rarely multiple nuclei. Cell inclusions are numerous in some fields. Cell outlines, as a rule, are quite sharp, but many cells blend with the stroma. Large and small areas of necrosis are present. Diagnosis.—Carcinoma of renal pelvis, malignancy grade IV.

Incidence.—Primary squamous-cell tumors of the kidney pelvis are relatively rare as approximately fifty-five cases have been previously reported. Walters estimates the ratio of squamous-cell epitheliomata to adeno-carcinomata to be between 1:11 and 1:14. As Patch has pointed out, there is a wide varia-

tion of terminology used. "Epithelioma, pavement epithelioma, cornifying epithelioma, squamous-cell carcinoma, epidermoidal carcinoma, and cancroid" are used to denote apparently the same tumor. This fact makes a statistical study of reported cases difficult.

Age Periods.—Kischensky observed the youngest patient, a woman aged thirty-two. Hedenius and Waldenstrom, and Simpson, both observed patients seventy-nine years old. The highest age incidence is in the fifth decade, in which 28 or 49 per cent. were noted. The average age of fifty-six cases is 55.67 years. The mean age is 55 years.

Sex.—Thirty-one were males and twenty-six were females. Location.—The tumor occurred twenty-six times on the left side, twenty-six times on the right side, while in five cases the side involved was not stated.

ETIOLOGY: Comparative Anatomy.—Wells refers to two instances of kidney tumors in animals. Baird and others report squamous-cell tumors of the kidney in fowls.

Experimental.—Pack and Buzzanca investigated the problem of the experimental production of epithelial hyperplasias by introducing sterile pebbles into the kidney pelvis of twenty-one adult rabbits. They concluded that hyperplasia of the transitional epithelium of the renal pelvis is a frequent and early response to the presence of renal stones. Benign villous papillomata of the renal pelvis occasionally follow irritation of renal stones and occur later than the more frequent simple epithelial hyperplasias. They also suggest that urinary stasis is one of the factors involved in tumor genesis within the renal pelvis. Richey believes that frequently repeated long-continued trauma produces malignant alteration in the tissues involved. Mucharinski's experiments coincided with Pack and Buzzanca's results, whereas Pavone produced only hyperkeratosis by the same methods.

Anomalies.—Three unusual cases of horse-shoe kidney with squamous-cell tumors are recorded. Primrose, in 1920, described the first case in a woman fifty-eight years of age. She was operated upon for stone in the right half of the kidney and a biopsy at that time showed the presence of tumor. More recently Willan reported a case in a fifty-six-year-old male in whom autopsy revealed a horse-shoe kidney with fusion of the lower pole and tumor metastasis to the pre-aortic lymph-nodes. Melen and Gaspar reported similar findings in a fifty-five-year-old man.

Trauma.—The authenticity of cases recording the occurrence of alleged trauma as a causative factor are to be critically questioned. Two such cases are recorded; one by Beneke and Namba, and another by Retzlaff.

Infection.—Pyuria was noted thirty-nine times. This was consistently present in the cases coëxisting with calculi and leukoplakia. This combination of infection and calculi led to the diagnosis of calculus pyonephrosis in most cases.

Leukoplakia.—The unusual coexistence of proved cases of leukoplakia with cancer of the kidney pelvis is recorded by Kischensky, Spiess, Walker, Patch, and Potts.

This subject was thoroughly studied by Kurtzmann, in 1929, who reviewed sixty-seven cases of leukoplakia of the kidney pelvis and concluded that leukoplakia may be the forerunner of squamous-cell cancer. From the analysis of his series he reported a coincidence of 11.9 per cent.; of these, six occurred in the kidney pelvis and two in the bladder. While leukoplakia may be a physiological metaplastic process, it may also become a pathological one in some cases. The carefully studied case of Patch demonstrated the transitional stages in the kidney pelvis. Multiple sections revealed an intermediary type, and while not definitely malignant was considered as pre-cancerous.

Potts studied twenty-six complete autopsy specimens in an effort to find squamous epithelium in the normal and in the infected urinary tracts not showing gross leukoplakia. No squamous epithelium was found and the variation from the normal transitional epithelium was accounted for by infection. He concluded that several etiological factors are probably responsible for this metaplasia, although the exact process is not clearly defined.

Wolbach and Howe noted in vitamin-A deficiency an extensive epithelial metaplasia. The epithelium was replaced by stratified keratinizing epithelium strongly resembling leukoplakia. A number of experimental rats with this disease died with obstruction in the urinary tract caused by occlusion with desquamated keratinized epithelial cells.

Leber reported an instance in an infant where cornified epithelium was found lining the pelvis of the kidney; a similar condition was found in the eye. He believed that the process was due to developmental changes in the urinary tract. Wilson offered the hypothetical suggestion that inclusions of ectodermal cells carried from the rectum to the kidney by way of the cloacal wall account for epidermoidal tumors of the kidney pelvis. The field of endocrine research may offer something new in this regard, as suggested by Von Borza in 1926.

Calculi.—Thirty of the fifty-seven cases or 52 per cent. of squamous-cell tumors of the kidney pelvis were associated with calculi. These reports showed that calculi varied greatly in number, size, and chemical structure. Multiple calculi were not unusual and the calculi are frequently of large size. Martin and Mertz concluded in their extensive review that the calculus was primary and the tumor secondary in fourteen or 63 per cent. of twenty-two cases of epithelial tumors of the pelvis and ureter. Of their series of 108 cases of kidney malignancy of all types associated with stone, they found that the average duration of symptoms from calculi was about nineteen years, and the symptoms relative to malignancy about five months. In Waterworth's case, the probable duration of stone was estimated to be twenty-eight years.

Battle's case gave a calculus history for six years, when nephrotomy was performed for stone and a benign papilloma was also removed. Eighteen months later left nephrectomy was done and a squamous-cell tumor was removed. This case demonstrates the probable transformation of a benign papilloma to epithelioma, as the result of long-continued trauma.

Diagnosis.—It is not possible to tabulate the initial symptoms in this series due to incomplete records. Bleeding is comparatively rare in contradistinction

to the papillary tumors, as these solid, often hornified, growths are relatively avascular. Hematuria and pyuria may precede the diagnosis of renal tumor by many years as illustrated in the cases of Scholl and Foulds and of Keynes. Preceding infection, leukoplakia, and calculi may account for these symptoms and is the usual diagnosis made. Pain is accounted for by renal dilatation and extension of the tumor. A palpable tumor mass indicates that ureteral obstruction has taken place with subsequent hydronephrosis or the parenchyma is involved by carcinomatous infiltration. In our second case peripheral extension to the cortex had occurred and in Case I infection had involved the perirenal tissues, producing a tumor mass which could be readily seen and palpated. Retrograde pyelography has greatly increased the accuracy of pre-operative diagnosis of renal pelvis tumors and excretory urography may be of further value. The distinction between papillary and nonpapillary kidney pelvis tumors is most difficult by pyelography. No pre-operative diagnosis of squamous-cell tumor has been made to date. In our second case the pre-operative diagnosis of primary kidney pelvis tumor was made.

Braasch clearly outlines the points in differential diagnosis and states that in every case of hematonephrosis the possibility of tumor of pelvic origin must be excluded.

In this series no diagnosis was made in eleven cases. Kidney tumor was diagnosed twenty times; kidney calculi twenty; pyonephrosis three; tuberculosis one, and cystic ovary one. Many cases were diagnosed only at autopsy, as was our Case I.

Pathology.—Thirty-one cases were classified as squamous-cell carcinoma; eleven epithelioma; nine pavement epithelioma; three epidermoid carcinoma; and one each as schirrous, epithelioma carcinoide, and "flat carcinomatous ulcer."

Cases without clinical data not included in our series are recorded by Coryell,⁵ Young,¹ Kaufman.¹ Other cases are recorded by Menetrier and Martinez, and others, who found squamous cells at the base of papillary tumors in the kidney pelvis. Marked epidermization has also been observed with calculus pyelitis and tuberculosis.

Ewing believes that excessive hornification must be regarded as a tendency inherent in the growth, as all cases are not associated with calculi or leukoplakia.

Hand and Broders describe four highly malignant squamous-cell epitheliomata of the renal cortex. In these cases there was no gross involvement of the renal pelvis. It is important to recognize this group as being distinct from the more common tumors of the pelvis.

Eleven graded cases are reported; Scholl and Foulds one case, grade high. Simpson four cases, all grade IV. Waterworth one case, grade IV. Potts one case, low grade. Scholl two cases, one grade II, and one grade IV. Our first case is a grade III tumor and our second case a highly malignant grade IV.

This review shows the histological grading to be uniformly high. The

only tumor of low malignancy was Potts' case which was also associated with leukoplakia.

Metastasis.—Twenty-four, or 42 per cent., of this series were observed at autopsy. In other cases exploratory operation proved the presence of metastasis. Clinical examination alone often revealed the presence of widespread disease, as for example in Hartmann's case.

Direct extension from the renal artery to the vena cava occurred five times, and to the local lymph-glands nine times. Bone metastasis were noted eight times. The adjacent vertebræ were involved five times, the seventh rib, the greater trochanter of the femur, and the lower end of the femur once each. The abdominal organs were involved as follows: liver, nine; adrenals, four; peritoneum, three; pancreas, two; ureter, two; and once each to the diaphragm, spleen, mesenteric lymph-glands, uterus and bladder. Thoracic organs were involved as follows: lungs six times, and heart twice. One instance of supraclavicular gland metastasis occurred.

Tumor plaques of the ureter found in our first case are also recorded by Taddei and Ewing.

TREATMENT: Surgical.—Only early surgical removal can save these patients. All writers agree that the diagnosis is made late in the course of the disease when the kidney is fixed or metastasis has already taken place. In several instances nephrotomy for stone was carried out and the presence of tumor was not suspected. In others only nephrotomy was done for drainage when the tumor was inoperable.

No operative procedure was done in eighteen cases. Operative procedures were carried out as follows: exploratory seven times, nephrotomy six times, and nephrectomy thirty-six times. In two cases, Battle, and Albarran and Imbert, two operations were carried out, first nephrolithotomy followed by nephrectomy.

The high incidence of 52 per cent. of associated calculi with squamous-cell tumors is to be emphasized from our study of this series. It would appear that the early prophylactic removal of kidney calculi should be recommended on these grounds if for no other reason.

Radiation.—In two cases, Simpson and our second case, post-operative radiation has been carried out following nephrectomy. In our case the kidney was removed, but tumor tissue was incised at the kidney pedicle. Walters gives great credit to the value of pre- and post-operative irradiation therapy. He describes cases where a fixed tumor diminished in size and became mobile, enabling later nephrectomy to be accomplished. In a recent five-year study he found 17 per cent. of forty-one inoperable kidney tumors of all types lived for more than five years.

Any attempt to get adequate dosage to kidney tumors by external irradiation is met with difficulties due to the depth of the tumor from the skin surfaces. Adequate interstitial irradiation with gold radon seeds is practically surgically impossible. Only with local extension at the hilus could such implantations

offer much aid and here the danger of placing active radium near large blood-vessels is great.

Prognosis.—In fifteen cases of this series the length of life and the cause of death are not stated. Eight cases are reported as "died." Six cases are reported as having recurrence after operation which caused death between six months and one year. Twenty-six patients died in the first six months after operation.

There are no five-year cures reported in this series. The fact that these tumors are generally of a high degree of malignancy and that clinically the diagnosis is made late combine to make this disease uniformly fatal.

SUMMARY.—(1) Two cases of squamous-cell carcinoma of the kidney pelvis are reported with a review of fifty-five cases from the literature.

- (2) The etiological factors are discussed with special reference to chronic irritation, especially infection, leukoplakia, and calculi. The removal of these factors is a definite prophylactic measure as all three conditions are closely associated with the presence of these highly malignant tumors.
- (3) Early surgical removal is indicated. Treatment by irradiation therapy is advocated, but no conclusive results can be stated.
 - (4) The prognosis is grave; no five-year cures are reported.

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Chronological List of Fifty-Seven Reported Cases of Primary Squamous-Cell Tumors of the Kidney Pelvis

CASE I, Hedenius and Waldenstrom, 1877–1878.—A male, aged seventy-nine. No operation was performed. At autopsy a primary carcinoma of the left renal pelvis and ureter with calculus was found, and extension along the renal vessels to the abdominal aorta vena cava and to the promentory of the sacrum.

Case II, Kundrat, 1891.—A male, aged forty-nine. Kidney tumor showed epithelial pearls. A large branching calculus was also present.

CASE III, *Ibid.*—A male, aged fifty-six. Nephrectomy was performed and a pathological diagnosis of epidermoid carcinoma made.

CASE IV, Giordano, 1892.—A female, aged fifty-seven. A pre-operative diagnosis of renal calculus with infection of the right kidney was made. Right nephrectomy disclosed an epidermoid carcinoma.

CASE V, Hildebrandt, 1894.—A female, aged forty-eight. A right nephrectomy revealed a pavement epithelioma.

CASE VI, Battle, 1895.—A male, aged fifty-one. A left nephrolithotomy was done for stone and infection. Later nephrectomy revealed a squamous carcinoma which recurred.

CASE VII, Kirschensky, 1901.—A female, aged thirty-two. Pavement epithelioma of the right kidney found at autopsy associated with infection and *leukoplakia*. Metastasis to lower end of right femur, liver, diaphragm, peritoneum, and lymph-nodes. She died five and a half months from onset.

Case VIII, Albarran and Imbert, 1903.—A male, aged sixty. Nephrolithotomy for calculus and infection on a diagnosis of calculus pyonephrosis, later followed by nephrectomy which revealed epithelioma carcinoide. He died two months post-operative.

CASE IX, Hartman, 1904.—A male, aged fifty-five. A left nephrectomy showed an infection and an epithelioma. He died of recurrence.

CASE X, *Ibid.*—A male, aged forty-six. A left nephrectomy was performed on a diagnosis of kidney tumor. A pavement epithelioma was found. He died four months post-operative, or three and a half years from onset. Autopsy showed a generalized carcinomatosis.

Case XI, Retzlaff, 1904.—A male, aged forty-three. Exploratory laparatomy for left kidney tumor, a pavement epithelioma was found. He died post-operative; the total duration of the disease was eight months. Autopsy disclosed extension to the spleen, tail of pancreas and left supraclavicular nodes.

CASE XII, Oraison, 1905.—A female, aged fifty. A left nephrotomy for calculus was done on a diagnosis of calculus pyonephrosis. A pavement epithelioma was found. Patient died three days post-operative.

CASE XIII, Besenbruch, 1907.—A female, aged fifty-nine. A left nephrectomy for kidney tumor with infection disclosed squamous carcinoma. She suffered a recurrence one year post-operative.

CASE XIV, Taddei, 1908-1909.—A male, aged forty. A right nephrectomy was done for calculus pyonephrosis and a pavement epithelioma was found. He died three days post-operative. Autopsy revealed tumor occluding the ureter and the vena cava.

CASE XV, Blum, 1909.—An "old male patient." He died soon after admission, an autopsy revealed a large kidney tumor (side not stated), which proved to be a pavement epithelioma, associated with branching phosphatic calculi.

CASE XVI, Scheel, 1910.—A male, aged thirty-seven. Exploratory laparatomy for right kidney tumor disclosed a pavement epithelioma. He died one month post-operative. Autopsy showed metastasis about kidney in omentum, adrenal, liver, diaphragm and lungs.

CASE XVII, Luys, etc., 1910.—A female, aged fifty-one. Nephrectomy for kidney tumor (side not stated) disclosed a pavement epithelioma. Patient died post-operative and an autopsy revealed metastasis in lymph-nodes near the vena cava.

CASE XVIII, Bauer, 1911.—A male, aged sixty-nine. No clinical details. At autopsy a scirrhous carcinoma with metastasis to liver, heart, lungs and bone (seventh rib and second lumbar vertebra). Patient died about one year from onset.

CASE XIX, Beneke and Nanba, 1911.—A male, aged forty-five years. A left nephrotomy and later a nephrectomy revealed a "flat carcinomatus ulcer." He died eleven months following an injury. Autopsy showed metastasis in the liver and the lungs, and tuberculosis in the bronchial glands.

CASE XX, Scalone, 1911-1912.—A male, aged thirty-nine. A right nephrotomy was done for calculus and pyonephrosis and a pavement epithelioma was found.

CASE XXI, Stusser, 1912.—A female, aged sixty-six. A left nephrectomy was done on a diagnosis of cystic ovaries. A pavement epithelioma was found. Patient died two months post-operative. Autopsy revealed metastasis along vena cava and in liver. The tumor eroded the first and second lumbar vertebræ, and the greater trochanter of the left femur.

CASE XXII, Beneke, 1915.—A female, aged fifty-five. Left nephrectomy was done revealing a pavement carcinoma. Autopsy disclosed extension to the adrenal and the spine, with thoracic kyphosis due to bone involvement.

CASE XXIII, Spiess, 1915.—A female, aged fifty-four. Left nephrectomy for kidney tumor in the presence of infection, calculus, and *leukoplakia*. A squamous carcinoma was found which recurred in seven months.

CASE XXIV, Primrose, 1920.—A female, aged fifty-eight. Right nephrectomy in the presence of calculus and *horse-shoe kidney*. Squamous carcinoma was found and the patient died eight months post-operative.

CASE XXV, Davis, 1922.—A female, aged sixty-two. Left nephrectomy done for kidney tumor, and a squamous carcinoma found. Patient died three weeks post-operative.

CASE XXVI, Ewing, 1922.—A female, aged fifty-eight. No clinical data. Nephrectomy revealed a squamous carcinoma. At autopsy the ureter was involved to the bladder, with metastasis in the uterus, mesenteric and aortic lymph-nodes.

CASE XXVII, Wells, 1922.—A male, aged fifty-seven. Nephrotomy for stone was done on a diagnosis of calculus pyonephrosis. Kidney showed squamous carcinoma with calculus. Patient died one day post-operative. Autopsy showed extension to adrenal retroperitoneal lymph-glands and peritoneum.

CASE XXVIII, Scholl and Foulds, 1924.—A male, aged sixty-two. Right nephrectomy for kidney tumor revealed squamous carcinoma of high malignancy with a calculus.

CASE XXIX, *Ibid.*—A female, aged fifty-three. Right nephrectomy for kidney pelvis tumor showed a squamous carcinoma with calculus. Patient died eleven days post-operative.

CASE XXX, *Ibid.*—A male, aged fifty-four. Right nephrectomy for kidney tumor showed squamous carcinoma with calculus. Patient died two months post-operative. Autopsy disclosed metastasis in liver and regional lymph-glands.

CASE XXXI, *Ibid.*—A male, aged fifty-four. Right nephrectomy for calculus showed calculus with squamous carcinoma. Patient died two months post-operative.

CASE XXXII, *Ibid.*—A male, aged sixty-four. Left nephrectomy for kidney infection, squamous carcinoma found. Patient died several months post-operative.

CASE XXXIII, Wheeler, 1924.—A female, aged thirty-six. Left nephrectomy was done for calculus, squamous carcinoma also found.

CASE XXXIV, Danforth, 1924.—A female, aged sixty-four. Right exploratory operation for renal tumor disclosed a squamous carcinoma. Patient died ten days post-operative. Autopsy showed metastasis to bladder over the ureteral orifice and extension into the vena cava.

CASE XXXV, Keynes, 1924.—A male, aged thirty-five. Right nephrectomy for calculus pyonephrosis showed also squamous carcinoma. Patient died eleven months post-operative of recurrence. Autopsy disclosed metastasis in right ventricle of heart and local recurrence.

CASE XXXVI, Walker, 1927.—A male, aged sixty-three. Right nephrectomy for calculus showed also leukoplakia and squamous carcinoma.

CASE XXXVII, Fumagalli, 1928.—A male, aged fifty-three. Laparotomy for pyloric obstruction. Later a right nephrectomy for calculus. Epidermoid carcinoma found.

CASE XXXVIII, Willam, 1928.—A male, aged fifty-six. Right nephrotomy for calculus pyonephrosis, squamous carcinoma also found. Patient died one day post-operative from heart attack. Autopsy disclosed horse-shoe kidney with fusion of lower poles, and metastasis to aortic lymph-glands.

CASE XXXIX, Herman and Greene, 1929.—A male, aged fifty-one. Right nephrectomy for infected kidney tumor disclosed non-papillary carcinoma with extension to the mesenteric glands. Patient died at operation.

Case XL, Patch, 1929.—A male, aged forty-seven. Cystotomy and biopsy of bladder tumor was done. Patient died six months post-operative. Autopsy showed the left kidney contained a squamous carcinoma with *leukoplakia* and calculus. There was leukoplakia of the entire urinary tract, also a squamous carcinoma of the bladder with calculus and calculi in the right kidney and ureter.

CASE XLI, Morton, 1929.—A male, aged forty-nine. Right nephrectomy for calculus pyonephrosis showed also epidermoid carcinoma. He lived three months post-operative. Autopsy showed metastasis to liver, lungs and vertebral erosion.

CASE XLII, *Ibid.*—A female, aged fifty-eight. Left nephrectomy for kidney tumor disclosed a squamous carcinoma with calculus.

CASE XLIII, Bowen and Bennett, 1930.—A male, aged fifty-seven. Left nephrectomy

for calculus disclosed also squamous carcinoma. Recurrence developed six months postoperative.

Case XLIV, Melen and Gaspar, 1931.—A male, aged fifty-five. Left nephrotomy for calculus disclosed also squamous carcinoma in a horse-shoe kidney. Patient died three weeks post-operative of septicæmia. Autopsy showed metastasis in regional lymphnodes.

CASE XLV, Price and Jacobs, 1931.—A male, aged fifty-four. Left nephrectomy for calculus hydronephrosis disclosed a squamous carcinoma.

CASE XLVI, Darmady, 1931.—A female, aged fifty-nine. A left nephrotomy for pyonephrosis disclosed squamous carcinoma with calculus. Patient died two months post-operative, or ten years after first symptom of kidney disease. Autopsy showed metastasis to liver and peritoneum and extension to spine and muscles.

CASE XLVII, Simpson, 1931.—A female, aged seventy-nine. Right nephrectomy for kidney tumor and hydronephrosis disclosed a sessile epithelioma, grade IV.

CASE XLVIII, *Ibid.*—A female, aged sixty-four. Right nephrectomy for calculus and kidney tumor and hydronephrosis disclosed a sessile epithelioma, grade IV. Patient died two hours post-operative.

CASE XLIX, *Ibid.*—A female, aged fifty-seven. Exploratory laparotomy disclosed a left kidney tumor, sessile epithelioma, grade IV. Patient died several months post-operative.

CASE L, *Ibid.*—A female, aged sixty-nine. Right nephrectomy for kidney tumor and pyonephrosis disclosed a sessile epithelioma, grade IV. Patient was alive and well six months post-operative.

CASE LI, Rabinovitch, 1932.—A female, aged sixty-four. A left nephrectomy for tuberculosis and ureteral stricture revealed a squamous carcinoma which occluded the renal artery by tumor thrombus with resulting complete infarction of the kidney.

Case LII, Waterworth, 1932.—A male, aged sixty-four. Right nephrectomy for calculus disclosed also squamous carcinoma, grade IV. Patient died five and one-half months post-operative. Probable duration of calculus twenty-eight years.

Case LIII, Potts, 1932.—A female, aged sixty-seven. Right nephrotomy for calculus and infection disclosed also squamous carcinoma of low grade with *leukoplakia*. Patient died five years following operation for primary renal calculus. Autopsy revealed no metastasis.

Case LIV, Scholl, 1933.—A female, aged fifty-seven. Left ureterotomy for stone, later nephrectomy disclosed squamous carcinoma, grade IV. Patient died two months post-operative. Autopsy showed metastasis in both lungs, adrenals, pancreas, liver, and retroperitoneal lymph-nodes.

CASE LV, *Ibid.*—A female, aged sixty-seven. Right exploratory operation for calculus pyonephrosis disclosed squamous carcinoma, grade II. Patient died one month post-operative.

CASE LVI, (Author's Case I).—A female, aged fifty-six. Drainage of right perinephritic abscess. Patient died five days post-operative. Autopsy disclosed squamous carcinoma, grade III, with calculus and infection and tumor implants along ureter with extension to aortic lymph-glands.

CASE LVII, *Ibid.* (Case II).—A male, aged fifty-four. Left nephrectomy for kidney pelvis tumor disclosed squamous carcinoma, grade IV. Patient received high voltage X-ray therapy but died of recurrence four months post-operative.

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